# Concentrations of persistent organic pollutants in blood of the Spanish population: Temporal trend

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#### **Abstract**

The present article reviews the human biomonitoring studies conducted in Spain to assess exposure to persistent organic pollutants (POPs) such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), polybrominated diphenyl ethers (PBDEs), and per- and polyfluoroalkyl substances (PFAS). In general terms, important variations in POPs concentrations between Spanish regions and specific populations were observed, while no associations between exposure to POPs and adverse health outcomes were found. Moreover, occupational exposure seems not to be a risk factor with regards to POPs exposure in the Spanish population. The present review highlights the importance of conducting human biomonitoring studies to find possible associations between POPs and adverse health effects.

**Keywords**: Human exposure, human biomonitoring studies, blood samples, Spanish population, POPs

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#### Introduction

Persistent organic pollutants (POPs) are a large group of carbon-based compounds which have a high lipophilicity and low water solubility (1,2). Additionally, they are highly resistant to degradation, which leads to an accumulation in the environment and a biomagnification along the food chain (3,4). POPs include a wide range of compounds such as polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), polybrominated diphenyl ethers (PBDEs), and per- and polyfluoroalkyl substances (PFAS), among others (5). Newer POPs include also polychlorinated naphthalenes (PCNs), hexabromocyclododecanes (HBCDs), and dechlorane plus (DP) (6).

Human exposure to these type of compounds leads to adverse health outcomes, such as disruptive effects in the endocrine, reproductive or immune systems, as well as neurotoxicity and genotoxic effects (7–9). Due to these detrimental health effects, it is essential to know the current exposure levels of the general population, so actions can be taken by policy makers in order to ensure that the population's health is not at risk. The present paper aims to review the available scientific literature on the current exposure levels of POPs in the blood of the Spanish population, as well as to establish the temporal trend.

### Search strategy

PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and Scopus (https://www.scopus.com) were used as scientific databases. The search was carried out using the following search string:

(""Dioxins"" [MeSH Terms] OR ""dioxin" [All Fields] OR ""Dioxins" [All Fields] OR ""pcdds""[All Fields] OR ""Furans""[MeSH Terms] OR ""Furans""[All Fields] OR ""furan""[All Fields] OR ""pcdd fs""[All Fields] OR (""Polychlorinated Biphenyls'"'[MeSH Terms] OR "'Polychlorinated Biphenyls'"'[All Fields] ""polychlorinated biphenyl""[All Fields] OR ""pcb""[All Fields]) OR (""Halogenated Diphenyl Ethers'" [MeSH Terms] OR "Halogenated Diphenyl Ethers'" [All Fields] OR ""Halogenated Diphenyl Ethers""[All Fields] OR ""pbde""[All Fields]) OR (""perfluorinated alkylated substances""[All Fields] OR ""perfluorinated alkylated substances""[All ""pfas""[All Fields]) Fields] OR OR (""polychlorinated naphthalene'"'[All Fields] OR ""polychlorinated naphthalenes""[All Fields] ""pcn""[All Fields]) OR (""polychlorinated diphenyl ethers""[All Fields] ""polychlorinated diphenyl ether" [All Fields])) AND (""Blood" [MeSH Terms] OR ""Blood""[All Fields] OR ""Serum""[MeSH Terms] OR ""Serum""[All Fields] OR ""Plasma""[MeSH Terms] OR ""Plasma""[All Fields]) AND (""Humans""[MeSH Terms] OR ""Humans""[All Fields] OR ""human""[All Fields] OR ""human population" [All Fields]) AND (""Spain" [MeSH Terms] OR ""Spain" [All Fields])"

Up to 80 peer-reviewed articles were used for the current review, divided for the different sections as follows: a) 59 for PCBs; b) 10 for PFAS; c) 10 for PBDEs and d) 16 for PCDD/Fs.

# Polychlorinated biphenyls (PCBs)

PCBs are one of the most frequently analysed organochlorine compounds (OCs), mainly due to their widespread exposure and detection around the world. In Spain, several studies have quantified the levels of PCB congeners – especially 138, 153 and 180 – and determined their association with a number of diseases. The temporal variation of PCBs 138, 153 and 180 is summarized in Table I.

**Table I** A summary of concentrations of various persistent organic pollutants (POPs) in the Spanish populations: Temporal variations.

**Tabela I** Pregled koncentracija različitih dugotrajnih organskih zagađujućih supstanci (POPs) među stanovništvom Španije: vremenske varijacije.

Pollutant	Concentrations	Reference	Most recent concentrations	Reference
PCB 138	Whole blood: 0.49 ng/mL	- González et al. (1998) -	Plasma: 32.9 ng/g lipid	Henríquez-Hernández et al. (2021)
PCB 153	Whole blood: 0.67 ng/mL		Plasma: 49 ng/g lipig	
PCB 180	Whole blood: 0.59 ng/mL		Plasma: 43.6 ng/g lipid	
PFOS	Maternal serum: 6.99 ng/mL Cord serum: 1.86 ng/mL	- Manzano-Salgado et al. (2015)	Maternal plasma: 6.1 ng/mL	– Carrizosa et al. (2021) –
PFOA	Maternal serum: 2.97 ng/mL Cord serum: 1.90 ng/mL		Maternal plasma: 2.4 ng/mL	
PFNA	Maternal serum: 0.85 ng/mL Cord serum: 0.32 ng/mL		Maternal plasma: 0.7 ng/mL	
PFHxS	Maternal serum: 0.84 ng/mL Cord serum: 0.40 ng/mL		Maternal plasma: 0.6 ng/mL	
∑PBDEs	Maternal serum: 12 ng/g lipid Paternal serum: 12 ng/g lipid Cord serum: 17 ng/g lipid	Gomara et al. (2007)	Maternal serum: 8.19 ng/g lipid Cord serum: 4.11 ng/g lipid	García-Villarino et al. (2020)
∑PCDD/Fs	Blood of residents near a MSWI: 13.5 pg I-TEQ/g lipid Blood of residents far a MSWI: 13.4 pg I-TEQ/g lipid	González et al. (1998)	Plasma: 6.79 pg I-TEQ/g lipid	Nadal et al. (2019)

Some studies belong to the INMA project (Infancia y Medio Ambiente – Environment and Childhood), which focuses on studying the role of the most important environmental pollutants during pregnancy and the beginning of life, including the effects

on child growth and development. Alvarez-Pedrerol et al. (2009) selected 1090 pregnant women from Sabadell (Catalonia) and Gipuzkoa (Basque Country) and analysed the levels of PCB 28, 118, 138, 153 and 180 in serum samples. Median levels of PCB 138, 153 and 180 were 18.8, 34.5 and 23.6 ng/g lipid, respectively, while PCB 28 and 118 were below the limits of detection (LOD). Forns et al. (2012) analysed the levels of 7 PCB congeners (28, 52, 101, 118, 138, 153 and 180) in cord blood from pregnant women (n = 355) and in the blood from their children (n = 278) at 4 years of age. Congeners 28, 52 and 101 could not be quantified in any of the samples of either cord or whole blood. Median levels for congeners 118, 138, 153 and 180 were 0.06, 0.14, 0.18 and 0.13 ng/mL for cord blood, and 0.09, 0.18, 0.25 and 0.12 ng/mL for whole blood samples. Correlations with poor neuropsychological development were not found (11).

Recently, Abellan et al. (2019), included 1308 mother-child pairs and analysed the levels of PCB congeners 138, 153 and 180 in the cord blood and their possible association with the lung function. The median levels of PCB 138, 153 and 180 were 0.08, 0.11 and 0.08 ng/mL, respectively. However, they were not associated with a decreased lung function in children at 4 and 7 years of age. The most recent study from the INMA cohort analysed 155 maternal serum samples and 229 cord blood samples to determine the levels of 5 PCB congeners (101, 118, 138, 153 and 180) (García-Villarino et al., 2020). Maternal serum showed concentrations of 5.23, 10.33, 37.1, 66.07 and 48.28 ng/g lipid for congeners 101, 118, 138, 153 and 180, respectively. On the other hand, cord serum PCB levels were the following: 33.12 ng/g lipid for PCB-101, 6.76 ng/g lipid for PCB-118, 32.55 ng/g lipid for PCB-138, 47.7 ng/g lipid for PCB-153 and 27.79 ng/g lipid for PCB-180. Additionally, some PCBs were correlated with feminizing effects in males and masculinizing effects in females aged 4 (13).

Gascon et al. (2012) based their study on three different cohorts from the INMA project (Sabadell, Gipuzkoa and Valencia). A total of 1455 mother-children pairs were recruited between 2004 and 2008, and maternal serum was analysed for PCB-118, -138, -153 and -180. The highest PCB concentrations were found for congener 153 (45.1 ng/g lipid), followed by congener 180 (32.5 ng/g lipid), congener 138 (27.1 ng/g lipid) and congener 118 (6.4 ng/g lipid). However, no association between PCBs and lower respiratory tract infections was found (14). In the same three cohorts - but recruited between 2003 and 2008 - Gascon et al. (2013) assessed the prenatal exposure to PCB-153, which is the PCB congener with the highest levels and detection rate in the study. The geometric mean found in maternal serum samples was 39.81 ng/g lipid, which is similar to that found in their previous study (14). A year later, Gascon et al. (2014) assessed the correlation between exposure to PCBs and respiratory health. In this case, a cohort from Menorca (Balearic Islands) was used. It consisted of 482 mothers who visited antenatal care between 1997 and 1998. Participants were divided into two study populations (A and B), with levels of  $\Sigma$ PCBs in cord blood of 0.58 and 0.59 ng/mL, respectively. Notwithstanding, no associations between PCBs and altered respiratory function were found (16).

In turn, Ibarluzea et al. (2011) measured the levels of 7 PCB congeners (28, 52, 101, 118, 138, 153 and 180) in serum samples from 1259 pregnant women. Only the geometric means of PCB 138, 153 and 180 were determined (21.83, 38.92 and 26.99 ng/g lipid), as detection rates of the other congeners were very low (less than 5%). On the other hand, Llop et al. (2010) conducted a study with 541 pregnant women from the INMA Cohort of Valencia. In that study, PCB congeners 118, 138, 153 and 180 were measured in serum samples. The median levels were as follows: 10.69 ng/g for PCB-118, 30.41 ng/g for PCB-138, 45.74 ng/g for PCB-153 and 34.58 ng/g for PCB-180. Lopez-Espinosa et al. (2010) included in their study 453 infants, also from the INMA Cohort of Valencia. They measured the concentrations of PCB-118, -138, -153 and -180, with the highest median levels corresponding to PCB-153 (46 ng/g lipid), followed by PCB-138 (34 ng/g lipid), PCB-180 (33 ng/g lipid) and PCB-118 (23 ng/g lipid). The same research group investigated the relationship between 4 PCB congeners (118, 138, 153 and 180) in cord blood samples from the INMA-Valencia cohort and the birth size (n=494) (20). The median levels were 0.062 ng/mL for PCB-118, 0.085 ng/mL for PCB-138, 0.113 ng/mL for PCB-153 and 0.082 ng/mL for PCB-180. However, there was no association between PCB exposure and the birth size of new-borns (20). In another study conducted by this research group, PCB congeners 138, 153 and 180 were analysed in 2369 samples of maternal serum, and in 1140 cord serum samples of four Spanish cohorts from the INMA project (Asturias, Gipuzkoa, Sabadell and Valencia) (21). In both kinds of samples, PCB-153 was the congener showing the highest concentrations (0.28 and 0.12 ng/mL for maternal and cord blood, respectively). PCB-180 showed lower levels than PCB-153 (0.20 and 0.08 ng/mL for maternal and cord blood, respectively), while PCB-138 showed similar concentrations as PCB-180 (0.17 and 0.08 ng/mL for maternal and cord blood, respectively) (21). Llop et al. (2017) measured the levels of PCBs in 1128 samples from pregnant women from the INMA cohorts of Valencia and Sabadell and assessed their association with the thyroid system. PCB-153 showed the highest concentration (0.22 ng/mL) again, followed by PCB-180 0.15 ng/mL and PCB-138 (0.13 ng/mL). No correlations between PCBs and thyroid hormone levels were found (22).

Morales et al. (2013) analysed the levels of 4 congeners (118, 138, 153 and 180) in serum samples from 2031 pregnant women. Serum concentrations were 7.6 ng/g lipid for PCB-118, 24.8 ng/g lipid for PCB-138, 40.9 ng/g lipid for PCB-153, and 28.8 ng/g lipid for PCB-180. In a previous INMA Cohort-related study, the maternal levels of 5 PCB congeners (28, 118, 138, 153 and 180) were measured in 584 pregnant women from the Sabadell cohort (24). PCB-118 was the congener with the lowest median levels (12.1 ng/g lipid), while PCB-153 showed the highest concentrations (35.5 ng/g lipid). PCB-138 and -180 had concentrations of 21.1 and 25.9 ng/g lipid, respectively. None of the samples showed detectable levels of PCB-28 (24). In a cohort of 344 children, Valvi et al. (2012) associated the levels of 7 PCBs congeners (28, 52, 101, 118, 138, 153 and 180) in cord blood samples with overweight at 6.5 years. As in previous studies, PCB-28, -52, -101 and -118 had the lowest detection rates (5, 11, 28% and 76%, respectively) and the lowest mean levels (0.07, 0.05, 0.04 and 0.06 ng/mL, respectively), while PCB-138, -150 and -150 a

180 were the most detected congeners (95, 98 and 95%, respectively), and also those with the highest concentrations (0.14, 0.18 and 0.13 ng/mL, respectively). Moreover, authors found an association between childhood overweight and PCB exposure in girls (25). Taking into account that the most detected congeners are 138, 153 and 180, Valvi et al. (2014) measured these PCBs in maternal serum collected in the first trimester of pregnancy (n=1285), with the following results: 22.8 ng/g lipid for PCB-138, 38.8 ng/g lipid for PCD-153 and 27.9 ng/g lipid for PCB-180. Similarly, Vizcaino et al. (2011) measured the levels of 7 PCB congeners (28, 52, 101, 118, 138, 153 and 180) in cord blood samples from 265 newborns recruited from two Mediterranean cohorts of the INMA project (Menorca and Valencia). In both cohorts, median levels of PCB-28, -52 and -101 were below the LODs. Reported median levels in Valencia for PCB-118, -138, -153 and-180 were 0.03, 0.06, 0.08 and 0.06 ng/mL, respectively, while for Menorca they were 0.08, 0.16, 0.17 and 0.12 ng/mL, respectively (27).

The BIOAMBIENT.ES project is another national Spanish project, where 1936 subjects residing in all 17 Spanish Autonomous Communities and the autonomous city of Ceuta were recruited between 2009 and 2010. In a study performed by Huetos et al. (2014), serum samples from 1880 subjects were analysed for PCB contents. Median values for men were: 35.25 ng/g lipid for PCB-138, 47.78 ng/g lipid for PCB-153 and 62.97 ng/g lipid for PCB-180. Similar results were found for women: 34.31 ng/g lipid for PCB-138, 45.57 ng/g lipid for PCB-153, and 55.06 ng/g lipid for PCB-180. Regarding specific levels in each Autonomous Community, the Basque Country had the highest PCB concentration, while the Canary Islands showed the lowest exposure (28). In a recent study of the BIOAMBIENT.ES project, Arrebola et al. (2019) investigated the exposure to PCBs in a specific cohort with diagnosed hyperuricemia (n=950). Although 6 congeners were determined (28, 52, 101, 138, 153 and 180), three of them (28, 52 and 101) were below the limit of quantification (LOQ). Median levels of congeners 138, 153 and 180 were 34.45, 45.14 and 58.30 ng/g lipid, which were very similar to those reported by Huetos et al. (2014). Furthermore, serum concentrations of PCB-138 and -153 were associated with an increased risk of hyperuricemia (3).

The EPIC-Spain (European Prospective Investigation into Cancer and Nutrition) study cohort included 41438 healthy volunteers – between 29 and 69 years of age – who were recruited from 1992 to 1996 in five regions of Spain: Asturias, Gipuzkoa and Navarra from the north, and Granada and Murcia from the south of the country. Agudo et al. (2009) measured the serum concentrations of PCBs in individuals from the general population (n=953). The median concentrations of congeners 118, 138, 153 and 180 were 34.4, 104.6, 182.6 and 119.5 ng/g lipid, respectively. Exposure to PCBs was higher in northern Spain than in the southern regions (29).

On the other hand, the MCC-Spain study is a population-based multicase-control survey conducted between 2009 and 2013 in 12 Spanish Provinces. The main objective of this project was to study the factors related to some of the most relevant tumours in the Spanish population. In this sense, Fernández-Rodríguez et al., (2015) determined the serum concentrations of PCBs in a study that included 312 participants from various

Provinces (Barcelona, Madrid, Cantabria and Navarra). All three congeners (138, 153 and 180) had detection rates over 92%, with values of 95.30 ng/g lipid for PCB-138, 96.65 ng/g lipid for PCB-153, and 71.18 ng/g lipid for PCB-180 (30).

The ENCA nutritional survey is a regional project conducted between 1997 and 1998 in the Canary Islands, where 783 subjects – from 6 to 75 years – participated in the blood extraction part. Henriquez-Hernández et al. (2011) analysed 607 serum samples for the detection of 7 PCB congeners (28, 52, 101, 118, 138, 153 and 180). The median concentration of PCB-153 was 21.8 ng/g lipid, and 6.7 ng/g lipid for PCB-180. The remaining PCB congeners (28, 52, 101, 118 and 138) were not detected (31). In a subsequent study, Henríquez-Hernández et al. (2014) conducted the analysis of 7 PCB congeners (28, 52, 101, 118, 138, 153 and 180) in plasma samples of 428 adults aged  $\geq$ 18 years. The median levels for PCB-153 and PCB-180 were 32.1 μg/L and 9.40 μg/L, respectively. Although 7 congeners were analysed, only those with a detection rate higher than 50% were reported. In another study with the same cohort conducted by Boada et al. (2014), 607 serum samples were analysed to measure the levels of the same 7 PCB congeners. Similarly, results were only reported for PCB-153 and -180, their median levels being 0.04 and 0.01 μg/L, respectively. More recently, Henríquez-Hernández et al. (2017) measured the concentrations of the 7 PCB congeners in 429 plasma samples. More than 77% of the samples had detectable levels of congeners 153 and 180, with median values of 0.2 and 0.1 μg/L, respectively. These concentrations were significantly higher among subjects having diabetes (33). Other studies not related to the ENCA survey were conducted in the Canary Islands. Henríquez-Hernández et al. (2016) recruited 100 people living in these Islands and compared their PCB levels with 131 Moroccans, who were recruited 2 months within their arrival to the Islands. In this case, 6 PCB congeners were assessed, and their levels for the Canarian and Moroccan individuals were as follows: PCB-28 (8.9 vs 16.3 ng/g lw, respectively); PCB-52 (4.9 vs 3.3 ng/g lw, respectively); PCB-101 (8.2 vs 3.3 ng/g lw, respectively); PCB-138 (4.9 vs 3.3 ng/g lw, respectively); PCB-153 (9.8 vs 8.1 ng/g lw, respectively) and PCB-180 (6.5 vs 4.9 ng/g lw, respectively). In a recent survey conducted by Henriquez-Hernández et al. (2021), the levels of PCBs were measured in 463 participants from the PREDIMED-Canarias cohort. The general median concentrations of the three PCB congeners were as follows: 32.9 ng/g lipid for PCB-138, 49 ng/g lipid for PCB-153 and 43.6 for PCB-180. Prenatal exposure to PCBs in newborns from the Canary Islands was also assessed in a study conducted by Cabrera-Rodríguez et al. (2020), in which 447 cord blood samples were analysed for 18 PCBs congeners (28, 52, 77, 81, 101, 105, 114, 118, 123, 126, 138, 153, 156, 157, 167, 169, 180 and 189). General detectable concentrations ranged between 0.001 ng/mL (PCB-28, -118, -126 and -138) and 2.129 ng/mL (PCB-28). PCB-57 was not detected in any of the samples.

Another regional survey (Catalan Health Interview Survey) was conducted in Catalonia between 2001 and 2002, in which only adult subjects (18-74 years) were recruited. A total of 1374 individuals completed the survey and the health examination, which also included the extraction of urine and blood samples. A subsample of 919

subjects was selected by Porta et al. (2010) to analyse 7 PCB congeners. Four of the seven congeners (118, 138, 153 and 180) had detection rates over 85%, with values of 22.8, 69.5, 100.1 and 77.3 ng/g lipid, respectively, while PCBs 28, 52 and 101 showed a much lower detection rate – between 11.7 and 22.5% - with values of 1.6, 0.2 and 0.2 ng/g lipid, respectively (37). The same research group compared the PCB values obtained from Barcelona residents in 2002 (37) with PCB levels from samples collected in 2006 (38). The concentrations of PCB congeners in 2002 were as follows: 30.8 ng/g lipid for PCB-118, 91.9 ng/g lipid for PCB-138, 121.9 ng/g lipid for PCB-153 and 95.6 ng/g lipid for PCB-180, while those of PCBs in 2006 were 13.5 ng/g lipid for PCB-118, 48.3 ng/g lipid for PCB-138, 68.6 ng/g lipid for PCB-153 and 63.4 ng/g lipid for PCB-180. Thus, the levels of the most detected PCB congeners were reduced by between 34 and 56% (38). Gasull et al. (2012) studied the relationship between PCB concentration and diabetes and prediabetes in the CHIS cohort. A total of 886 participants were selected for that study, the results for the general population being: 0.133 ng/mL for PCB-118, 0.451 ng/mL for PCB-138, 0.625 ng/mL for PCB-153 and 0.501 ng/mL for PCB-180. Moreover, an increasing concentration of PCBs was associated with diabetes and prediabetes (39).

Other Catalan studies were conducted in different population groups. In Flix (Tarragona, Catalonia), a hospital-based case-control study was performed to assess the correlation between the exposure to environmental contaminants and the risk of colorectal cancer (40). A total of 220 subjects were randomly selected from a cohort of 866 participants, which were recruited between 1996 and 1998. The levels of PCB-28 and PCB-52 were below the LODs, while those of PCB-118, PCB-138, PCB-153 and PCB-180 were 92, 308, 362 and 252 ng/g lipid, respectively. An association between the risk of colorectal cancer and PCB congeners 28 and 118 was observed (40). In a general population cohort, Wingfors et al. (2000) compared the levels of PCBs for Spain and Sweden. Mean values of the  $\Sigma$ PCBs were 1310 ng/g for the Swedish population and 1450 ng/g for the Spanish population, with congener profiles varying between countries. In general, the higher chlorinated congeners were more dominant in the Spanish group than in the Swedish one (41). Ribas-Fitó et al. (2002) conducted another study in the region of Flix with children born between 1997 and 1999. PCBs were measured in 70 cord serum samples. The median concentrations found in cord serum were: 0.01 ng/mL for PCB-118, 0.05 ng/mL for PCB congeners 138, 153 and 180 (∑PCBs= 0.27 ng/mL). Ribas-Fitó et al. (2003) also analysed and compared the levels of total PCBs in maternal serum between 1994 (n=85) and 1997-1999 (n=40). The median value of  $\Sigma$ PCBs in 1994 was 1.4 ng/mL, whereas in 1997-1999 was 1.9 ng/mL. This means that the concentration was 35% higher, but not significantly different (43). Similarly, Sala et al. (2001) evaluated the levels of PCBs in 72 maternal blood samples and 69 cord blood samples collected between 1997 and 1999 in a rural area belonging to Flix and nearby areas. The geometric means of the  $\Sigma$ PCBs in maternal blood were 1.64 ng/mL, and 0.36 ng/mL for cord blood, which are similar to those reported for the same area (42,43). Recently, Junqué et al. (2020) also conducted a study with pregnant women from Tarragona Province. In this case, 50 subjects were recruited between 2016 and 2017 from Reus (Tarragona Province), and

maternal serum – from the first trimester and at delivery – and cord blood were collected to analyse 7 PCBs. PCB congeners 28 and 118 were not detected in any of the samples, while the highest level corresponded to PCB-180 and PCB-153. The median levels in maternal serum in the first trimester were 0.005 ng/mL for PCB-52, 0.001 ng/mL for PCB-101, 0.048 ng/mL for PCB-138, 0.11 ng/mL for PCB-153 and 0.073 ng/mL for PCB-180. On the other hand, the levels at delivery were 0.005 ng/mL for PCB-52, 0.001 ng/mL for PCB-101, 0.06 ng/mL for PCB-138, 0.21 ng/mL for PCB-153 and 0.13 ng/mL for PCB-180. In cord serum, the levels of PCB-52, -101, -138, -153 and -180 were 0.01, 0.001, 0.033 and 0.011 ng/mL, respectively (45).

Catalonia is an autonomous community that has a great industrial activity, including various municipal solid waste incinerators (MSWI) and a hazardous waste incinerator (HWI), which could be an important source of exposure to polychlorinated compounds such as PCBs. Various studies have been conducted in the area of influence of these incinerators in order to assess the exposure of the general population and the occupationally-exposed population. Domingo et al. (2001) assessed the baseline exposure to PCBs when the HWI (Constantí, Tarragona County) started its industrial activity. A total of 28 workers in the new facility were recruited and plasma samples were analysed. The geometric means of PCB congeners 28, 52, 101, 138, 153 and 180 were 12.9, 7.5, 7.1, 129, 182 and 158 ng/g lipid, respectively. According to the authors, the levels of exposure were of the same order of magnitude as those previously found in a nonoccupationally exposed population from Mataró (Catalonia) – where a MSWI is located and whose PCBs concentration were analysed in 201 adults (47). The levels for congeners 101, 138, 153 and 180 were 0.04, 0.49, 0.67 and 0.59 ng/mL, respectively. Congeners 28 and 52 were not detected in any of the samples (47). Since the first study (46), periodical surveys were carried out to monitor the internal levels PCBs in workers from the HWI. Thus, Schuhmacher et al. (2002) assessed the levels of PCBs in plasma samples from 23 workers, one year after the HWI started its regular activities. No differences in PCB levels between the baseline study and one year after were found in any of the three workplaces considered (plant, laboratory and administration) (48). In contrast, after three years of regular operations, the levels of PCBs 28, 52, 101, 138 and 153 were significantly lower in plasma samples from 28 workers of the HWI when compared to those of the baseline study (49). A similar trend was also reported by Mari et al. (2007), who again assessed the exposure to PCBs a few years later. The reported median values for congeners 28, 52, 101, 138, 153 and 180 were 1.6, 0.3, 0.9, 46.5, 105 and 110 ng/g lipid, respectively. These results showed a significant decrease (p<0.01) when compared to the levels of the baseline study conducted by Domingo et al. (2001). Eight years after the beginning of the operations in the plant, Mari et al. (2009) re-assessed the exposure in 29 workers. Plasma levels of PCBs 28, 52 and 101 were significantly lower than their respective control values, while congeners 138, 153 and 180 had decreased notably, but not significantly. The last study to evaluate the concentration of PCBs in the workers of the HWI was carried out by Mari et al. (2013). All the PCB congeners analysed (28, 52, 101, 138, 153 and 180) were significantly lower (p<0.05)

than those found in the baseline study (52). All the studies conducted in the HWI located in Tarragona showed that there were no evident signs of occupational exposure to PCBs.

In Mataró, Gonzalez et al. (2000) monitored the levels of PCBs in residents living near the MSWI two years after regular operations. PCBs 28 and 52 were not detected, neither in 1995, nor in 1997, in any of the samples. In 1997, general PCB exposure increased in both groups of residents – living near and further away from the MSWI – by 25 and 12%, respectively. Furthermore, minimal changes were observed among workers of the MSWI (53). Parera et al. (2013) carried out a temporal study to monitor the PCB levels in blood samples from the general population – both exposed and non-exposed. In 2012, the potentially exposed group had a concentration of PCBs of 0.52  $\mu$ g/g fat and the control groups from Mataró and Arenys de Mar (a village near Mataró) showed concentrations of 0.65 and 1.16  $\mu$ g/g fat. Furthermore, the workers from the MSWI showed a concentration of 0.71  $\mu$ g/g fat. No significant differences were observed between groups (54).

The PANKRAS II study is also a regional project that was conducted between 1992 and 1995 at five general hospitals of eastern Spain, where 185 patients with exocrine pancreatic cancer were recruited. In a study performed by Porta et al. (1999), a cohort of 51 subjects were selected among the PANKRAS II cohort to evaluate the association between selected PCBs and the mutations in codon 12 of the K-ras gene. The highest median values were found for PCB-180 (1.56 ng/mL), followed by PCB-138 (1.45 ng/mL) and PCB-153 (1.31 ng/mL). Patients with K-ras mutation had significantly higher concentrations of these three congeners when compared to the wild-type cases (55). Some years later, Porta et al. (2008) compared the levels of PCBs with the social class of 135 subjects. Authors found that these compounds were higher in the less affluent occupational classes, meaning that social class could not be independent of the risk of pancreatic cancer.

Regarding eastern Spain, other individual studies have been carried out. A population-based birth cohort was established in Menorca (Balearic Islands) that included 259 children born between 1997 and 1998 (Álvarez-Pedrerol et al., 2008). Median levels of PCB congeners 28, 52, 101, 118, 138, 153 and 180 were 0.01, 0.03, 0.08, 0.10, 0.17, 0.25 and 0.12 ng/mL, respectively. The authors suggested that exposure to PCB compounds might affect the thyroid system, specifically T3 levels (57). In Valencia, another eastern city, an association between thyroid levels and PCB exposure was assessed in pregnant women (n=157) (58). The sum of total PCBs was 0.85 ng/mL, which is similar to that reported by Álvarez-Pedrerol et al. (2008) (0.78 ng/mL). By contrast, no association was found between PCB exposure and thyroid hormone levels (58).

In southern Spain, exposure assessment studies to PCBs have also been conducted. Arrebola et al. (2014) studied the association between PCB exposure and obesity in a population from Granada. Three congeners (138, 153, and 180) were determined in 298 serum samples from a cohort recruited between 2003 and 2004. The median levels were 80.63 ng/g lipid for PCB-138, 237.45 ng/g lipid for PCB-153, and 184.34 ng/g lipid for PCB-180. The results suggested a potential relationship between PCB exposure and

obesity (59). The same authors also studied exposure to PCBs in 107 women diagnosed with gestational diabetes mellitus (60). The median values for congeners 138, 153 and 180 were 0.26, 0.73 and 0.31 ng/mL, respectively. The authors suggested that exposure to certain POPs was a modifiable risk factor that contributes to insulin resistance (60). In turn, Artacho-Cordón et al. (2015) recruited 103 women diagnosed with breast carcinoma from Granada and evaluated their exposure to PCBs in serum samples. Median values were 0.12 ng/mL for PCB-138, 0.10 ng/mL for PCB-153 and 0.14 ng/mL for PCB-180. These results are lower – but of the same order of magnitude – than those reported by Arrebola et al. (2015). On the other hand, González-Alzaga et al. (2018) assessed exposure to PCB-138, -153 and -180 in 305 children living in farming communities from Almería, another Southern city from Spain. Median values for PCB-138, -153 and -180 were 0.2, 0.36 and 0.34 ng/mL, which are similar to those found by Artacho-Cordón et al. (2015) and Arrebola et al. (2015).

In the North of Spain, namely in the Basque Country, various studies have also been carried out to determine exposure to PCBs. In a general population cohort, Aurrekoetxea Agirre et al. (2011) assessed the exposure to PCBs in the vicinities of a lindane plant that produced hexachlorocyclohexane (HCH) (n=424). The geometric means of PCBs were: 14.2 ng/g lipid for PCB-118, 61.3 ng/g lipid for PCB-138, 88.4 ng/g lipid for PCB-153 and 88.5 ng/g lipid for PCB-180. No significant correlations were found between control and potentially-exposed groups (63). Similarly, Zubero et al. (2009) evaluated the baseline exposure to PCBs in the population residing near a MSWI that started its regular activities in 2005. Serum samples of 283 subjects were analysed to determine the content of PCBs. All samples had detectable levels of congeners 138, 153 and 180, while for congener 118, the detection rate was 42.8%. The highest levels were found for PCB-153 (95.02 ng/g lipid), followed by PCB-180 (84.93 ng/g lipid), PCB-138 (66.17 ng/g lipid) and PCB-118 (7.70 ng/g lipid) (64). These results were similar to those previously reported by Aurrekoetxea Agirre et al. (2011). In turn, Zubero et al. (2015) assessed the temporal trend of PCB concentrations in the general population, not related to the MSWI and living in areas near to and further away from the facility. Two cross-sectional samples were obtained from 162 volunteers with a gap of two years (2006 and 2008). Geometric means in 2006 were 68, 93.8 and 85.6 ng/g lipid for PCBs 138, 153 and 180, while in 2008 the concentrations were 64.8, 92.4 and 92.4 for the same PCBs, respectively. PCB-138 levels were significantly lower, while PCB180 concentrations were significantly higher in 2008. No significant differences were found for PCB-153 (65). Subsequently, Zubero et al. (2017) recruited 127 individuals to assess, once more, the impact of residing near the MSWI. The median levels were 0.54 ng/g lipid for PCB-28, 0.34 ng/g lipid for PCB-52, 0.29 ng/g lipid for PCB-101, 4.07 ng/g lipid for PCB-138, 10.74 ng/g lipid for PCB-153 and 12.99 ng/g lipid for PCB-180. Changes in total sum of PCBs throughout the years (2006, 2008 and 2013) showed a significant decrease, when comparing 2006 and 2013 (254.06 vs 32.36 ng/g lipid) (66).

## Per- and polyfluoroalkyl substances (PFAS)

PFAS are resistant to thermal, chemical and biological degradation due to their strong bonds. Their properties make them ideal for use in many consumer products. Therefore, their presence is widespread around the world. The temporal variation of PFOS, PFOA, PFNA and PFHxS is summarized in Table 1. In Spain, some national studies have been carried out to determine the levels of exposure to PFAS, specifically the BIOAMBIENT.ES project and the INMA project. The former includes two studies. Bartolomé et al. (2017) measured PFAS exposure in a subset of 755 serum samples from the BIOAMBIENT.ES cohort. The levels of perfluoroctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorohexane sulfonate (PFHxS) and perfluorodecanoic acid (PFDA) were determined. The median levels of PFAS were the following: 7.55 ng/mL for PFOS, 2.03 ng/mL for PFOA, 0.82 ng/mL for PFHxS, 0.92 ng/mL for PFNA and 0.36 ng/mL for PFDA. Subjects living in Catalonia and Galicia had the highest serum values, while for most PFAS the lowest values corresponded to the Canary Islands (67). Arrebola et al. (2019) correlated the exposure between PFAS and the risk of hyperuricemia in 342 samples. The median levels of PFOS, PFOA, PFNA, PFHxS and PFDA were 7.23, 1.34, 0.88, 0.73 and 0.35 ng/mL, respectively, which are very similar to those previously reported by Bartolomé et al. (2017). Regarding hyperuricemia, only PFOA was associated with an increased risk of suffering from this adverse health condition (3).

Regarding the INMA project, several studies have been conducted in recent years. In 2015, Manzano-Salgado et al. (2015) used a subset of the regional cohorts from Valencia and Sabadell (n=66) to determine the levels of PFAS in pregnant women during the first trimester and delivery. Maternal plasma showed levels of 0.79, 6.18, 2.85 and 0.84 ng/mL for PFHxS, PFOS, PFOA and PFNA, respectively. Similarly, maternal serum had concentrations of 0.84, 6.99, 2.97 and 0.85 ng/mL for the same compounds, respectively. Lower levels were found in cord serum, with 0.40 ng/mL for PFHxS, 1.86 ng/mL for PFOS, 1.90 ng/mL for PFOA and 0.32 ng/mL for PFNA (68). Manzano-Salgado et al. (2016) also included three regional cohorts from the INMA study (Gipuzkoa, Sabadell and Valencia) recruited between 2003 and 2008 (n=1216). The results were the following: 0.58, 6.05, 2.35 and 0.65 ng/mL for PFHxS, PFOS, PFOA and PFNA, respectively. These median values are similar to those previously reported by the same authors (68). Manzano-Salgado et al. (2017a) also evaluated the associations between prenatal exposure to PFAS and birth outcomes in 1202 mother-child pairs. Mean levels were 0.58 ng/mL for PFHxS, 6.05 ng/mL for PFOS, 2.35 ng/mL for PFOA and 0.66 ng/mL for PFNA. In general, PFAS levels were not associated with birth outcomes. Only PFHxS, PFOA and PFNA showed a weak, but non-significant correlation with reduced birth weight (70). The same authors assessed the associations between prenatal exposure to PFAS and cardiometabolic risk (71). Geometric mean was 0.61 ng/mL for PFHxS, 5.80 ng/mL for PFOS, 2.32 ng/mL for PFOA and 0.66 ng/mL for PFNA. Nonetheless, PFAS exposure was not associated with an increased cardiometabolic risk (71). In turn, Matilla-Santander et al. (2017), studied the association between PFAS and

metabolic outcomes in 1240 pregnant women from three regions of the INMA project (Gipuzkoa, Valencia and Sabadell). The highest median values were found for PFOS (6.05 ng/mL), followed by PFOA (2.35 ng/mL), PFNA (0.65 ng/mL) and PFHxS (0.58 ng/mL). PFOS and PFHxS were positively associated with impaired glucose tolerance, as well as with gestational diabetes mellitus. PFOA was positively associated with total cholesterol, while PFOS and PFNA were negatively correlated with triglycerides (72). Recently, Costa et al. (2019) assessed the possible associations between PFAS exposure and foetal biometry in a subset of 1230 mother-child pairs from the INMA cohort. PFHxS, PFOA, PFOS and PFNA medians were the same than those reported by Matilla-Santander et al. (2017). In general terms, there were no associations in any trimester of pregnancy (73). Finally, using the same cohort and the same PFAS values, Carrizosa et al. (2021) associated PFAS exposure to the neuropsychological development of the foetus. Higher prenatal exposure to PFAS was associated with a worse motor development at 14 months, especially to PFHxS. In addition, a marginal positive correlation between general cognitive development at 4-5 years and PFOS, was observed (74). In a study conducted in Tarragona (Catalonia) belonging to the HEALS project, the levels of PFOS and PFOA in 50 pregnant women were measured (75). Mean plasma levels of PFOA were 0.45, 0.13 and 0.12 ng/mL at the first trimester, at delivery and in cord plasma, while those of PFOS were 2.93, 2.21, and 1.17 ng/mL, respectively. These results are lower than those reported by other authors in pregnant women (68–74).

## Polybrominated biphenyl ethers (PBDEs)

PBDEs are compounds used as flame retardants additives, due to their capacity to react with gas-phase free radicals during combustion. They are chemically stable and might accumulate in the food chain. The temporal variation of  $\Sigma$ PBDEs is summarized in Table 1. Within the INMA project, several studies have been conducted to assess exposure to PBDEs in pregnant women and in children. Carrizo et al. (2007) analysed 13 PBDE congeners (17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183 and 190) in 92 cord blood samples, and in serum from 4-year-old children. The average concentration of the sum of PBDEs was 6.2 and 4.3 ng/g lipid in new-borns and in 4-year-old children, respectively. BDE-47 showed the highest concentrations (2.8 and 2.9 ng/g lipid in cord blood serum and serum, respectively). Several years later, Gascon et al. (2011) also analysed the levels of three congeners of PBDEs (47, 99 and 100), which showed the highest concentrations in the study conducted by Carrizo et al. (2007). The median levels of BDE-47, BDE-99 and BDE-100 were 2.10, 0.38 and 0.38 ng/g lipid for cord blood, while for serum at age of 4 they were 0.12, 0.12 and 0.12 ng/g lipid, respectively. Results showed that postnatal exposure to BDE-47 was significantly related to an increased risk of symptoms of the attention deficit subscale of ADHD symptoms (77). Vizcaino et al. (2011b) determined the levels of PBDEs in a non-occupationally exposed mother-child pairs from the INMA-Valencia cohort (n=174). Total PBDE levels in umbilical cord serum and in maternal serum were 9.6 ng/g lipid for both matrices, being BDE-47 the congener with the highest concentration (2.3 ng/g lipid). The same authors evaluated the

prenatal exposure to PBDEs in two Mediterranean cohorts from Valencia and Menorca (27). A total of 265 new-borns were recruited and the levels of 5 PBDEs (47, 99, 100, 153 and 183) were measured. Total concentrations of PBDEs in Valencia cohort were 6.5 ng/g lipid, while in the Menorca cohort they were 2.8 ng/g lipid. In both cohorts, BDE-47 was the highest contributor to PBDE exposure, with the results being similar to those reported in other studies (76-78). In turn, Lopez-Espinosa et al. (2015) examined the relationship between PBDE exposure and foetal growth and new-born anthropometry in the INMA-Cohort (Asturias and Valencia). PBDE congeners (47, 99, 153, 154 and 209) were measured in serum of 670 mothers and in 534 umbilical cord samples. Levels of PBDEs in serum samples were 10.74 ng/g lipid, with a value of 7.51 ng/g lipid in umbilical cord samples. The authors reported inversely significant relations between PBDEs and abdominal circumference, estimated foetal growth, and biparietal diameter (79). The most recent study regarding PBDE exposure in the INMA cohort was carried out by García-Villarino et al. (2020). PBDE levels in maternal serum (n=155) and cord blood (n=229) were measured, and the effects on the anogenital distance (AGD) were assessed. Median levels of BDEs 28, 47, 99, 153, 154 and 209 in maternal serum were 0.16, 0.26, 1.63, 2.52, 2.60 and 1.02 ng/g lipid, respectively, while those found in cord serum were 0.31, 0.56, 0.50, 0.30, 0.57 and 1.87 ng/g lipid, respectively. Only an inverse association between anogenital index and BDE-209 was found in male children (13).

In the BIOAMBIENT.ES project, to date, only one study has reported the levels of PBDEs (28, 47, 99, 100, 153, 154 and 183) in 365 samples (3). BDEs 28, 99, 100 and 183 showed concentrations below the LOQ while BDE-47, -153 and -154 had quantifiable levels (0.06, 0.47 and 0.15 ng/g lipid, respectively). An inverse association between BDE-153 and the risk of hyperuricemia was detected, being positively associated with uric acid levels (3). In a CHIS-related study, Garí and Grimalt (2013) assessed the levels of 14 PBDE congeners in a Catalan cohort (n=731). The median concentration of the analysed congeners was 15.4 ng/g lipid, with BDE-209 and BDE-47 showing the highest contribution to total exposure (3.7 and 2.6 ng/g lipid, respectively) (80). Other regional studies were conducted in Madrid and in the Canary Islands. The former was conducted by Gómara et al. (2007), where 61 maternal serums, 51 paternal serums and 44 umbilical cord serums were analysed for 15 PBDE congeners. Median levels of  $\sum$ PBDEs were 12, 12 and 17 ng/g lipid for maternal, paternal and umbilical cord serum, respectively (81). In turn, Cabrera-Rodríguez et al. (2020) reported the levels of PBDEs in a cohort from La Palma (Canary Islands). BDE-85 was not detected in any of the samples, while the levels of other congeners ranged between 0.006 to 0.078 ng/mL (36).

### Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs)

PCDD/Fs are probably the most hazardous pollutants released by incinerators. They are very persistent in the environment and in the tissues of the exposed population. Therefore, most of the studies have been conducted around incinerator plants. The temporal variation of  $\Sigma$ PCDD/Fs is summarized in Table 1. In Tarragona County (Catalonia), the first study was carried out in 1999 during the construction of a new HWI

(46). The levels of PCDD/Fs in 28 workers of the HWI were analysed, with mean levels of 27.6 pg I-TEQ/g lipid (range: 13.4 – 84 pg I-TEQ/g lipid) (46). One year after starting the plant activities, Schuhmacher et al. (2002), assessed the levels of PCDD/Fs in 19 HWI workers. The results showed a mean concentration of 16.9 pg I-TEQ/g lipid, which is similar to that of the baseline survey (48). Six years after regular operations of the HWI, Mari et al., (2007) measured the concentrations of PCDD/Fs in blood samples from 19 workers in order to establish temporal variations with respect to the baseline study. The mean PCDD/Fs concentration was significantly lower than that found in the first study (10.4 pg I-TEQ/g lipid) (50). Later, the same research group, also determined the levels of PCDD/Fs in blood samples from workers of the HWI after 8 years of operations (n=19) (51). The decrease in PCDD/Fs levels was even more substantial when compared to the baseline study (2.5 vs. 27.6 pg WHO-TEQ/g lipid). Results indicated that there are no evident signs of occupational exposure to PCDD/Fs (51). Twelve years since the start of the activities of the HWI, Mari et al. (2013) analysed the concentrations of PCDD/Fs in blood samples from 18 workers. Similar values with respect to the previous survey were found (4.6 pg I-TEQ/g lipid) (52). Concurrently with the assessment of occupational exposure, the same research group also studied the exposure of the residents living near this facility. Schuhmacher et al. (1999) measured the baseline levels of PCDD/Fs in 20 subjects living in the vicinity of the new HWI. The mean PCDD/Fs value was 27.0 I-TEQ/g lipid with a range between 14.8 and 48.9 pg I-TEQ/g lipid (82). Three years after regular operations, Agramunt et al. (2005), studied the temporal variation in comparison to the baseline study in subjects living near the HWI (n=20). The authors found a significant reduction in PCDD/Fs with respect to the first survey (27.0 vs. 15.7 pg I-TEQ/g lipid) (83). Some years later, Nadal et al. (2008) also measured the levels of PCDD/Fs of non-occupationally exposed population (n=20). The authors reported a significant decrease with respect to the baseline study (27.0 vs. 9.36 pg I-TEQ/g lipid) (84). In 2012, a follow-up study was carried out by the same research group, where levels of PCDD/Fs were assessed in blood samples from 40 subjects (85). There was a further decrease of the exposure (6.18 pg I-TEQ/g lipid) when compared to the previous surveys (84,85). Finally, the last survey was conducted in 2018, and blood samples from 40 subjects were obtained (86). The level of PCDD/Fs for the non-occupationally exposed population was 6.79 pg I-TEQ/g lipid, which was significantly lower than the baseline concentration (27.0 pg I-TEQ/g lipid) but similar to those found in the two previous surveys (9.36 and 6.18 pg I-TEQ/g lipid) (86).

In Mataró, another Catalan city, two studies to assess human exposure around a MSWI were conducted. González et al. (1998) recruited 198 adults living near and far from the incinerator and assessed the exposure to PCDD/Fs. Mean PCDD/F levels were 13.5 and 13.4 pg I-TEQ/g lipid for subjects living near and far from the MSWI, respectively (47). Two years after regular operations, the same research group analysed the levels of PCDD/Fs in the same population groups (53). There was an increase of the PCDD/Fs concentrations in both groups, with them being 16.7 pg I-TEQ/g lipid for residents living close to or further of the MSWI. However, according to the authors, the

slight increase in the PCDD/Fs concentration was not due to the incinerator's emissions (53). Several years later, Parera et al. (2013) assessed the temporal trend of PCDD/Fs exposure around the MSWI in 104 exposed subjects and 97 non-exposed subjects randomly selected from Mataró. Mean levels of PCDD/Fs were 12.9 and 13.3 pg I-TEQ/g lipid for exposed and non-exposed populations (54).

In the Basque Country, various studies were also conducted to assess human exposure to PCDD/Fs around a MSWI. Zubero et al. (2009) analysed the levels of PCDD/Fs in pooled serum samples from residents living at a different distance from the plant. Median levels of PCDD/Fs were similar regardless of the zone: 24.3 and 27.3 pg WHO-TEQ/g lipid for Zone E1 and E2, which are located less than 2 km away from the plant; 21.3 pg WHO-TEQ/g lipid for Zone C1, which is located 5 km from the MSWI but with high-traffic density, and 18.8 pg WHO-TEQ/g lipid for Zone C2, which is an area located 20 km from the plant, and with minimal industrial and traffic activities. Total mean PCDD/Fs were 23.45 pg WHO-TEQ/g lipid (64). Two years later, the same research group, analysed the concentrations of PCDD/Fs in pooled serum samples again, and compared the results with those found in the previous survey (87). Mean PCDD/Fs levels in 2008 were 23.6 pg WHO-TEQ/g lipid, which are similar to those previously found (23.45 pg WHO-TEQ/g lipid) (87). Finally, in 2013, levels of PCDD/Fs were also measured in the same area (66). There was a significant decrease in the exposure to PCDD/Fs, with a mean level of 4.67 pg WHO-TEQ/g lipid (66).

#### **Conclusions**

The present article has reviewed the results published in the scientific literature regarding the levels of various POPs in the Spanish population, considering children, pregnant women, general population, as well as workers from industrial activities, basically waste incinerators. The results show that there is great variation among Spanish regions and populations, with no clear pattern of exposure and with the concentrations of PCBs being higher in the Northern regions than in the South. In general terms, there were no associations between POPs exposure and health effects. Only specific congeners were associated with some specific health outcomes, especially diabetes and obesity. Finally, there were no differences in POPs exposure – especially PCBs and PCDD/Fs – between occupationally and non-occupationally exposed populations. In summary, many human biomonitoring studies to assess POP exposure in the population have been conducted through the years in Spain, highlighting the importance of these surveys to disclose potential associations with several potential diseases.

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# Koncentracije perzistentnih organskih zagađivača u krvi stanovništva Španije: vremenski trend

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## Kratak sadržaj

U ovom radu je dat pregled studija humanog biomonitoringa koje su sprovedene u Španiji kako bi se procenila izloženost perzistentnim organskim zagađivačima (POPs) kao što su polihlorovani bifenili (PCBs), polihlorovani dibenzo-p-dioksini (PCDDs) i polihlorovani dibenzofurani (PCDFs), polibromovani difenil etri (PBDEs) i per- i polifluoroalkil supstance (PFAS). Uopšteno posmatrano, primećene su bitne varijacije u koncentraciji POPs supstanci među regionima Španije i među određenim grupama stanovništva, ali nije utvrđena povezanost između izloženosti POPs supstancama i štetnih posledica po zdravlje. Pored toga, čini se da izloženost POPs supstancama na radnom mestu nije faktor rizika među stanovništvom Španije. U radu se naglašava značaj izvođenja studija humanog biomonitoringa kako bi se otkrile moguće veze između izloženosti POPs supstancama i štetnih posledica po zdravlje.

**Ključne reči**: izloženost ljudi, studije humanog biomonitoringa, uzorci krvi, stanovništvo Španije, POPs